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Marked improvement in gastric involvement in Behçet's disease with adalimumab treatment

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ABSTRACT

Gastric involvement is the least frequent manifestation of Behçet's disease, and effective treatment for it unknown. Here the case of a patient with gastric involvement in Behçet's disease that was markedly improved with adalimumab therapy is presented. A 68-year-old man developed an oral ulcer, erythema, folliculitis, and arthralgia. Behçet's disease was suspected; then, prednisolone and colchicine were administered. Esophagogastroduodenoscopy showed a punched-out ulcer in the posterior wall of the gastric antrum. Ileocolonoscopy showed multiple punched-out ulcers in the terminal ileum. Capsule endoscopy showed multiple circular ulcers throughout the entire small intestine. A diagnosis of non-steroidal, anti-inflammatory, drug-induced enteritis was made. Withdrawal from diclofenac and initiation of lansoprazole healed the circular ulcers in the small intestine, but were ineffective for the gastric ulcer and punched-out ulcers in the terminal ileum. Eradication of Helicobacter pylori was also ineffective. A diagnosis of gastric involvement of Behçet's disease was then made, and the gastric ulcer became steroid-dependent. Mesalazine powder was ineffective, and the patient was intolerant to azathioprine. Adalimumab healed the gastric ulcer, and prednisolone was withdrawn. The outcome of the present patient suggests that adalimumab is effective in the treatment of gastric involvement in Behçet's disease.

Keywords: Behçet's disease, gastric ulser, adalimum

Case Report

INTRODUCTION

Intestinal Behçet's disease (BD) occurs in 16% of BD patients (1). It is known to have a poor prognosis, and anti-tumor necrosis factor (TNF)-alpha therapy is one of the few effective treatments (2,3). Most intestinal BD patients involve the ileum and showing punched-out ulcers; upper gastrointestinal involvement is rare. The diagnosis and treatment of gastric involvement in BD are unclear because it is the least frequent manifestation of BD. Here the case of a patient with gastric involvement of BD that was markedly improved with adalimumab treatment is presented.

CASE PRESENTATION

A 68-year-old man developed an oral ulcer, erythema, folliculitis, and arthralgia. BD was suspected, and he was treated with prednisolone (PSL) and colchicine. After four months, he was admitted to a hospital because of fever and epigastric pain. He had no relevant past history. His was taking 12.5 mg of PSL, 10 mg of colchicine, and 75 mg of diclofenac daily at that time. His temperature was 38°C, and his C-reactive protein (CRP) level was highly elevated (22.61 mg/dL). His other vital signs and laboratory data were unremarkable. Human leukocyte antigen B51 and the pathergy test were both negative. Esophagogastroduodenoscopy showed a punched-out ulcer, which was approximately 2 cm in size, in the posterior wall of the gastric antrum (Figure 1 a,b). Ileocolonoscopy showed multiple punched-out ulcers in the terminal ileum (Figure 1c). Pathological findings of biopsy specimens from the gastric and ileal lesions were non-specific and did not show any granulomas. Capsule endoscopy showed multiple circular ulcers throughout the entire small intestine (Figure 1d). Non-steroidal anti-inflammatory drug (NSAID)-induced enteritis was diagnosed. Withdrawal from diclofenac

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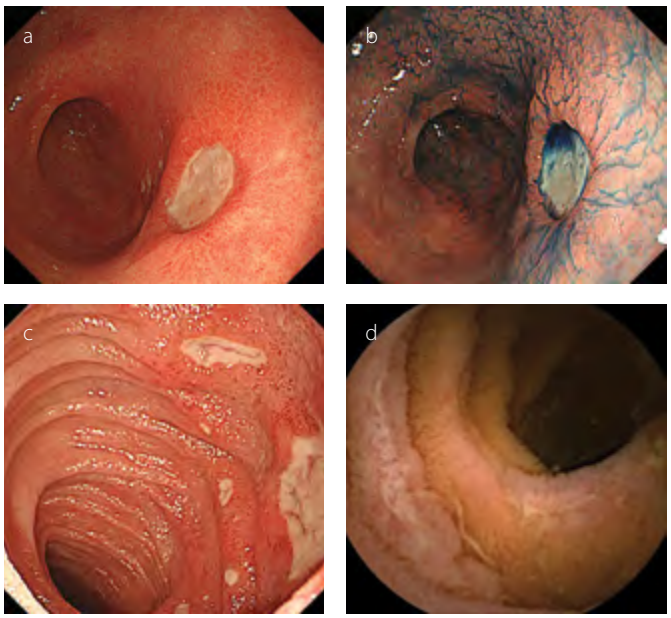

Figure 1. a-d. (a,b) Esophagogastroduodenoscopy showing a punched-out ulcer, which is approximately 2 cm in size, in the posterior wall of the gastric antrum. Gastric involvement in Behçet's disease was diagnosed because neither withdrawal from diclofenac nor Helicobacter pylori eradication was effective, (c) Ileocolonoscopy showing multiple punched-out ulcers in the terminal ileum. Intestinal Behçet's disease was diagnosed because withdrawal from diclofenac was ineffective, (d) Capsule endoscopy showing multiple circular ulcers throughout the small intestine. Non-steroidal anti-inflammatory drug-induced enteritis was diagnosed, and withdrawal from diclofenac healed these ulcers

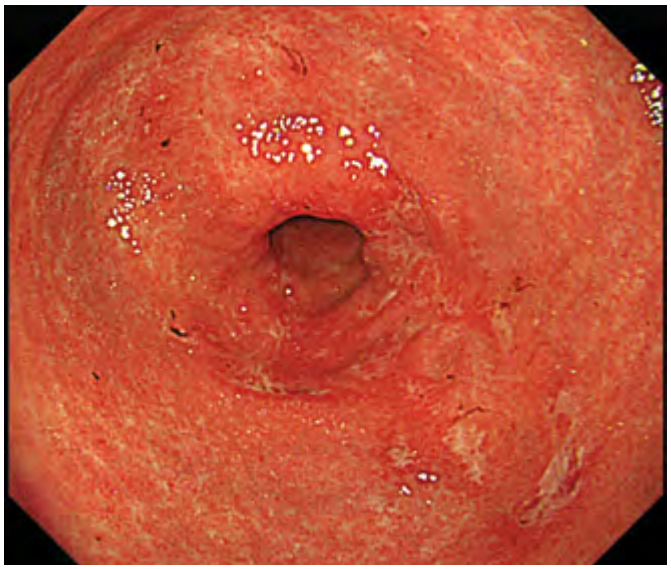

Figure 2. Esophagogastroduodenoscopy finding before initiating adalimumab. Gastritis worsened when the prednisolone dose was tapered to less than 10 mg

and initiation of rabeprazole immediately improved his symptoms and normalized his CRP level.

After two weeks, the circular ulcers in the small intestine were healed, but the gastric ulcer and punched-out ulcers in the terminal ileum were not improved. Successful eradication of Helicobacter pylori was confirmed by urease breath test, but was not

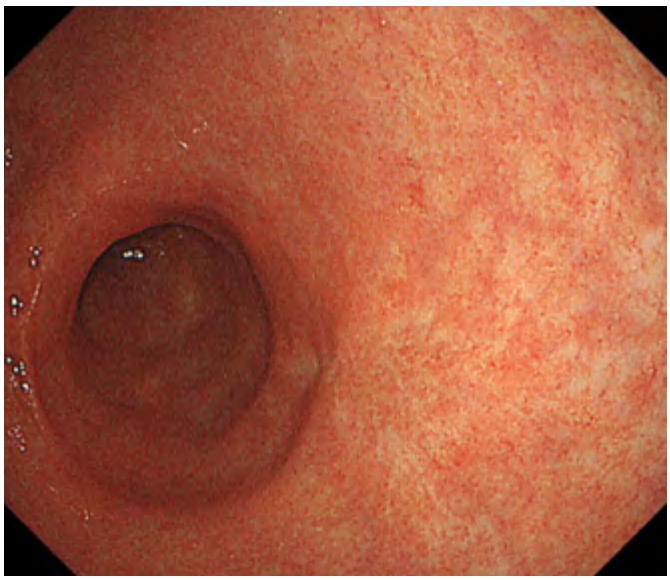

Figure 3. Nine months after the initiation of adalimumab. The ulcer has become scarred

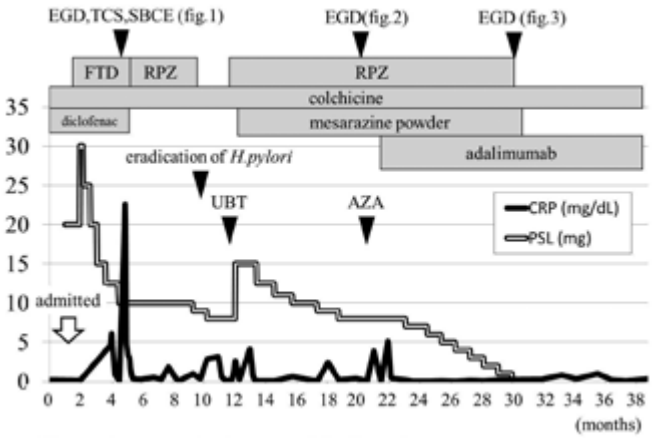

Figure 4. The clinical course of the present case. CRP level improved after withdrawal from diclofenac; however, it worsened when the prednisolone dose was tapered. Adalimumab normalized the CRP level, and prednisolone was withdrawn

CRP: C-reactive protein; EGD: esophagogastroduodenoscopy; ICS: ileo-colonoscopy; SBCE: small bowel capsule endoscopy; FTD: famotidine; RPZ: rabeprazole; NSAIDs: non-steroidal anti-inflammatory drugs; UBT: urease breath test; PSL: prednisolone; AZA: azathioprine

improved the gastric ulcer. The fever and epigastric pain recurred during tapering of the PSL dose, and the gastric ulcer did not improve. A diagnosis of gastric involvement in BD was then made, and dosage escalation of PSL to 30 mg/day improved his symptoms. The punched-out ulcers in the ileum became scarred, but the gastric ulcer did not heal. His symptoms then recurred repeatedly when the PSL dose was tapered to less than 10 mg. The gastric ulcer became steroid-dependent (Figure 2). Mesalazine powder was also ineffective. The patient was intolerant to 25 mg of azathioprine because of severe nausea and headache. Adalimumab (160 mg at week 0, 80 mg at week 2, and maintenance treatment with 40 mg every other week) improved his symptoms immediately, and PSL was withdrawn. Nine months later, the gastric ulcer became scarred (Figure 3). The patient's clinical course is outlined in Figure 4.

Written informed consent was obtained from the patient for the publication of this case report.

DISCUSSION

It is well known that the prevalence of BD is high in countries along the ancient Silk Road from the Far East through the Middle East to the Mediterranean. Japan is one of the countries with a high prevalence, but there are not many BD patients (The estimated prevalence is 13 to 20 per 100,000)(3). Intestinal BD is uncommon, occurring in 16% of BD patients in Japan (1). Gastric involvement is the least frequent manifestation of BD; the prevalence of gastric involvement is high prevalence in Taiwan (45%), but its overall prevalence is unknown (4,5).

To diagnose gastric involvement in BD, other stomach diseases must be excluded. This makes it difficult to diagnose. In fact, it was difficult to distinguish gastric involvement in BD from NSAID-induced enteritis and *H. pylori* infection in the present case. Gastric involvement in BD was diagnosed because neither withdrawal from diclofenac nor *H. pylori* eradication was effective.

In general, the prognosis of intestinal BD is poor, with death because of intestinal bleeding due to perforation occurring in some cases (5). Stenosis and perforation in patients with gastric involvement in BD have also been reported, though in small numbers (6-8). One of the reasons for its poor prognosis is the lack of clinical evidence and consensus for the management of intestinal BD due to the heterogeneity of the disease. Mesalazine, steroids, cyclosporine, anti-TNF alpha agents, azathioprine, colchicine, and thalidomide are used in the treatment of extra-intestinal BD and inflammatory bowel disease (5,9). The efficacy of anti-TNF alpha agents in treating BD have been reported (2). Adalimumab is one of the few evidence-based agents for treating intestinal BD in Japan (3). However, though its effectiveness has been shown in ileal involvement, treatment for gastric involvement in BD is still unclear. To the best of our knowledge, this is the first report of successful treatment of gastric involvement on BD. *H. pylori* eradication, proton pump inhibitor therapy, mesalazine powder, and colchicine were ineffective, and the patient became typically steroid-dependent. Adalimumab was effective, and PSL was withdrawn.

In conclusion, the outcome of the present case suggests that adalimumab is effective for the treatment of gastric involvement in BD.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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